

the insufficiency of available data to support the submission of a supplemental application for the new use, the data are persuasive to the extent that withholding the drug or device in a controlled study (e.g., by providing no therapy, a placebo, an alternative therapy, or an alternative dose) would pose an unreasonable risk of harm to human subjects. In assessing the appropriateness of conducting studies to support the new use, the manufacturer may provide evidence showing that the new use is broadly accepted as current standard medical treatment or therapy. The manufacturer shall also address the possibility of conducting studies in different populations or of modified design (e.g., adding the new therapy to existing treatments or using an alternative dose if monotherapy studies could not be conducted).

Subpart D—FDA Action on Submissions, Requests, and Applications

§ 99.301 Agency action on a submission.

(a) *Submissions.* Within 60 days after receiving a submission under this part, FDA may:

(1) Determine that the manufacturer does not comply with the requirements under this part and that, as a result, the manufacturer shall not disseminate any information under this part;

(2) After providing the manufacturer notice and an opportunity for a meeting, determine that the information submitted regarding a new use fails to provide data, analyses, or other written matter that is objective and balanced and:

(i) Require the manufacturer to disseminate additional information, including information that the manufacturer has submitted to FDA or, where appropriate, a summary of such information or any other information that can be made publicly available, which, in the agency's opinion:

(A) Is objective and scientifically sound;

(B) Pertains to the safety or effectiveness of the new use; and

(C) Is necessary to provide objectivity and balance; and

(ii) Require the manufacturer to disseminate an objective statement prepared by FDA that is based on data or other scientifically sound information available to the agency and bears on the safety or effectiveness of the drug or device for the new use; and

(3) Require the manufacturer to maintain records that will identify individual recipients of the information that is to be disseminated when such individual records are warranted due to special safety considerations associated with the new use.

(b) *Protocols/Studies.* Within 60 days after receiving a submission under this part, FDA shall:

(1) If the manufacturer has planned studies that will be needed for the submission of a supplemental application for the new use, review the manufacturer's proposed protocols and schedule for completing such studies and determine whether the proposed protocols are adequate and whether the proposed schedule for completing the studies is reasonable. FDA shall notify the manufacturer of its determination; or

(2) If the manufacturer has completed studies that the manufacturer believes would be an adequate basis for the submission of a supplemental application for the new use, conduct a review of the protocols submitted for such studies to determine whether they are adequate. FDA shall notify the manufacturer of its determination.

§ 99.303 Extension of time for completing planned studies.

(a) Upon review of a drug or device manufacturer's proposed protocols and schedules for conducting studies needed for the submission of a supplemental application for a new use, FDA may, with or without a request for an extension from the manufacturer, determine that such studies cannot be completed and submitted within 36 months. The agency may exercise its discretion in extending the time period for completing the studies and submitting a supplemental application. Extensions under this paragraph are not subject to any time limit, but shall be made before the manufacturer begins the studies needed for the submission of a supplemental application for the new use.

(b) The manufacturer may, after beginning the studies needed for the submission of a supplemental application for a new use, request in writing that FDA extend the time period for conducting studies needed for the submission of a supplemental application for a new use and submitting a supplemental application to FDA. FDA may grant or deny the request or, after consulting the manufacturer, grant an extension different from that requested by the manufacturer. FDA may grant a manufacturer's request for an extension if FDA determines that the manufacturer has acted with due diligence to conduct the studies needed for the submission of a supplemental application for a new use and to submit such a supplemental application to FDA in a timely manner and that, despite such actions, the manufacturer needs additional time to complete the studies and submit the supplemental application. Extensions under this paragraph shall not exceed 24 months.

(c) If FDA extends the time period for completing the studies and submitting a supplemental application under paragraph (a) of this section after the manufacturer has submitted a certification under § 99.201(a)(4)(ii)(B), or if FDA grants a manufacturer's request for an extension under paragraph (b) of this section, the manufacturer shall submit a new certification under § 99.201(a)(4)(ii)(B) that sets forth the timeframe within which clinical studies will be completed and a supplemental application will be submitted to FDA.

§ 99.305 Exemption from the requirement to file a supplemental application.

(a) Within 60 days after receipt of an application for an exemption from the requirement of a supplemental application, FDA shall approve or deny the application.

(1) If FDA does not act on the application for an exemption within the 60-day period, the application for an exemption shall be deemed to be approved.

(2) If an application for an exemption is deemed to be approved, FDA may, at any time, terminate such approval if it determines that the requirements for

granting an exemption have not been met. FDA shall notify the manufacturer if the approval is terminated.

(b) In reviewing an application for an exemption, FDA shall consider the materials submitted by the manufacturer and may consider any other appropriate information, including, but not limited to, any pending or previously approved applications for exemption submitted by the manufacturer.

(c) FDA may grant an application for an exemption if FDA determines that:

(1) It would be economically prohibitive for the manufacturer to incur the costs necessary to submit a supplemental application for a new use, which at a minimum requires:

(i) That existing data characterizing the safety and effectiveness of the drug or device, including data from the study described in the information to be disseminated are not adequate to support the submission of a supplemental application for the new use; and

(ii) That the cost of the study or studies for the new use reasonably exceeds the expected revenue from the new use minus the cost of goods sold and marketing and administrative expenses attributable to the new use of the product, and there are not less expensive ways to obtain the needed information; or

(2) It would be unethical to conduct clinical studies needed to support the submission of a supplemental application for the new use because:

(i) Existing data characterizing the safety and effectiveness of the drug or device, including data from the study described in the information to be disseminated are not adequate to support the submission of a supplemental application for the new use; and

(ii) Although available evidence would not support the submission of a supplemental application for the new use, the data are persuasive to the extent that withholding the drug or device in a controlled study would pose an unreasonable risk of harm to human subjects and no studies in different populations or of modified design can be utilized. In determining whether it would be unethical to conduct clinical studies, the agency shall consider, in addition to the persuasiveness of available evidence of effectiveness, whether